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BEDFORDSHIRE, MK43 0AH, UK

Patents ADP number (if you know it)

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64347 40003

4. Title of the invention

RECONFIGURABLE MICROFLUIDIC DEVICE

5. Name of your agent (if you have one)

LINDA TICWELL

CRANFIELD UNIVERSITY

"Address for service" in the United Kingdom
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SIL SOG

BEDFORDSHIRE, MK45 4DT, UK

Mervyn Ellis

404C House

23 Kingsway, London

109006

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FIELD OF THE INVENTION

The present invention relates generally to miniature instrumentation for chemical/biochemical analysis and chemical/biological sensing and, more specifically, to creating microchannels and controlled manipulations of fluids and capillaries in microchannels. These microchannels and tools for their creating and manipulation can be used in a variety of applications, including capillary electrophoresis, liquid chromatography, and flow injection analysis.

BACKGROUND OF THE INVENTION

Microfluidic systems have become increasingly popular tools in electronics, biotechnology, pharmaceutical and related industries where they provide numerous advantages, including significantly smaller reagent requirements, high speed of analysis and the possibility for automation [U.S. Pat No 6,251,343 and U.S. Pat No 6,379,974]. Typical examples of such microfluidic devices are a miniature gas chromatograph fabricated on a silicon wafer [Reference 1], a planar microcapillary electrophoresis chip [Reference 2, U.S. Pat. No. 4,908,112 and U.S. Pat. No. 6,309,602], a chip for separation and processing of nucleic acids [U.S. Pat. No 6,344,326] and microchips for the performance of amplification reactions [U.S. Pat. No 5,498,392], chemical and biological analysis [U.S. Pat. No 4,908,112 and U.S. Pat. No 6,342,142] and binding assay [U.S. Pat. No 5,637,469]. In microfluidic devices the transport and direction of materials, e.g., fluids, analytes and reagents within the microfabricated device, has generally been carried out by: (a) creating a pressure gradient; (b) the use of electric fields; (c) the use of acoustic energy. In order to fabricate microfluidic devices, the biotechnology and pharmaceutical industries have recently applied some of the same technologies that have proved effective in the electronics industry, such as photolithography, wet chemical etching, laser ablation, injection molding etc. As microfluidic systems become more complex, the ability to design and use them, including user handling

and system interfacing of such devices, becomes more and more difficult. It would therefore be desirable to provide an improved method for the design of flexible and reconfigurable microfluidic devices capable of being readily adapted to specific separation or analytical tasks and free from the problems associated with the current methods of production of such small-scale devices. The present invention meets these and a variety of other needs.

SUMMARY OF THE INVENTION

The present invention provides in general microfluidic devices that combine the advantages of microfluidics with improved material handling characteristics and reduced costs for manufacturing. The present invention accomplishes this by providing microfluidic devices that incorporate a body structure comprising a microchannel network disposed therein. The body structure has a plurality of ports disposed in it, where each port is in fluid communication with one or more channels in the channel network. It also contains either a plurality of electrodes connected to or integrated with one or more channels or another mechanism for directing thermal energy according to a set pattern. The microchannel network is created and maintained in the body structure by directing patterned energy flow, which results in partial melting of substrate material of interior part along the applied pattern.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic view of a microfluidic device according to a first preferred embodiment of the present invention.

FIG. 2 describes the formation of microchannel network in the interior part of the microfluidic device according to a second preferred embodiment of the present invention. A fluctuating laser (electronic or ionic beam) moves according to a predetermined pattern

defined by e.g. PC software and melts the substrate material of the interior part of the microfluidic device thus creating microchannels.

FIG. 3 describes formation of a microchannel network in the interior part of the microfluidic device. The energy flow emitted from broad energy source and patterned by mask melts the substrate material of the interior part of the microfluidic device and creates microchannels.

DESCRIPTION OF THE INVENTION

The present invention is generally directed to development of microfluidic systems and methods for their use. As used herein, the term "microscale" or "microfabricated" refers to features of a device, which have at least one structural element with dimension (e.g., depth, width, length, diameter, etc) in the range of from about 0.01 μm to about 1000 μm .

The first embodiment of the present invention describes a microfluidic device that comprises a body structure with a microchannel network disposed therein. Typically, the microfluidic device described herein comprises a top part, a bottom part, a side part and an interior part, wherein the interior part contains the microchannels as it is illustrated in FIG. 1. Typically the top and bottom parts of the device comprise a solid substrate that is substantially planar in structure. The side part of the device serves also for bonding together (and sealing) top and bottom parts and containing the interior part of the microfluidic device. The skilled artisan could design and use also essentially non-planar and stacked devices without deviating from the fundamental concept of the present invention.

The substrate materials used in the top, bottom and side parts of the microfluidic device are generally selected for their robustness under the conditions to which the microfluidic devices may be exposed, including organic solvents, buffers with different pHs, high and low temperature, irradiation and application of electric fields. Accordingly, in some preferred aspects, the substrate material may include materials such as glass, quartz, silicon or

polysilicon, silicon nitride, gallium arsenide, metals, their alloys, polymers, such as acrylates, methacrylates and oligourethanes, with non-exclusive examples of e.g. polymethylmethacrylate, polycarbonate, polyethylene, polypropylene, polyvinylchloride, polytetrafluoroethylene, polydimethylsiloxane, polysulfone, organometallic polymers, and composite materials consisting off, e.g. metals and silicon, polymers and glass.

The interior part of microfluidic devices comprises of substrate material with can be easily and reversibly changed from solid to liquid state by directing energy flow. Accordingly, in some preferred aspects, the substrate material will include water, organic solvents or gases, metals (e.g. gallium), organic and inorganic compounds, oligomers and polymers.

The microfluidic device prepared in accordance with the methods described herein, may contain a plurality of ports disposed in it, where each port is in fluid communication with one or more channels in the channel network and may also contain a plurality of electrodes connected/integrated with one or more channels. In some possible applications neither the ports for fluid communications nor the electrodes will be necessary (which means that the plurality in these cases will be "zero"). The ports and electrodes will have an external interface through the plurality of apertures/holes or connectors disposed through, e.g., top, bottom or side parts of the microfluidic device. In some applications the device will contain also holes, which function as reservoirs for reagents or wastes. In some applications the microfluidic devices will include an optical detection window(s) or detector(s), e.g. pH sensor, grating couple or surface plasmon resonance device, mass spectrometer, integrated into or linked with top, bottom or side parts of the device. In some aspects the ports for liquid communication will be used also as electrodes for current regulation.

In some designs the microfluidic device will contain a source of energy (light, heat, focused ionic, particle and electron beams, electromagnetic or microwave radiation) which delivers

reversible transformation of the substrate material in the interior part of the device from a solid to a liquid state.

In some another aspects of the present invention the microfluidic device also contains a heating/cooling device, heat exchanger or thermostat which maintains and controls the temperature in the microfluidic device, in particular in its interior part.

In some aspects the source of energy, heating and / or cooling of the device will be integral parts of the microfluidic device and in other aspects they will represent external modules.

In some other aspects the top, bottom or side parts will have integrated features as electric circuits or liquid crystals.

The second embodiment of the present invention describes the formation and maintenance of the integrated microchannel network in the interior part of the microfluidic device. This is achieved by patterned direction of energy, e.g. heat or light into the interior part of microfluidic device. This application of energy results in partial melting of the substrate material of the interior part of the device according to a preset pattern in a way that ensures that the liquid channels are formed between the top and the bottom parts of the device. In different formats of the microfluidic device the energy will be applied to the interior part in different ways, including using light (e.g. a laser beam), heat (using e.g. IR laser), focused ionic, particle, X-ray and electron beams. In some aspects the patterning will be achieved by focusing energy beams in pre-determined parts of the interior part through the transparent top (bottom or side) parts (Figure 2) or by using masks, which restrict the direction of energy to the predetermined areas of the interior part only (Figure 3). The advantages of the approach, described in this invention lies in the flexibility of the system. The pattern (and the patterned system of created microchannels) can be changed by re-focusing and re-directing the applied energy. The microchannel network will exist only when the energy is applied to corresponding areas. When the application of energy stops - the liquid in the channel will be

frozen and channel will disappear. A plurality of integrated microchannels, including transverse channels, cross intersections, "T" intersections, etc., in the same microfluidic device can be created for a variety of specific applications. The microchannel network can also be modified in real time during the analytical or separation method to facilitate or promote individual stages of the experiment or analysis. The connection between the channels, reservoirs, ports for fluid communications and electrodes can be easily established or terminated by focusing energy at appropriate connection points.

In some aspects the mask, top or bottom parts of the device will contain liquid crystals capable of changing their properties according to the applied current. In this case the microchannel patterning will be achieved by modulating the transparency of the liquid crystals and correspondingly by regulating local heating produced by energy passed through the liquid crystal. Yet in another aspects the mask, top or bottom parts will contain microcircuits capable of producing heat upon applying current. In this case the microchannels will be patterned according to structure of microcircuits and according to pattern of applied current.

The pattern can be created, changed and controlled by a computer using appropriate software. In some aspects the microfluidic device will be designed as a replaceable chip or stationary unit linked with samplers, liquid reservoirs etc.

The principle of creation and regulation of the channel network can also be used by the skilled artisan with nanoscale systems without deviation from the scope of the present invention.

The third embodiment of the present invention describes the manipulation of material to be transported (liquidified part of substrate material, solution, analytes, sample etc.) inside of the microchannel network, formed according to the pattern of applied energy. In preferred aspects, a controlled current applied to multiple electrodes will be used to effect material

transport. The connection between electrodes and channels will be established by directing energy to appropriate connection points. In another aspect the transport in microchannels will be regulated by applying a pressure gradient using external or integrated pumps. In yet another aspect the transport in microchannels will be regulated using acoustic energy or temperature gradient. In some aspects the transport of material will be regulated by freezing or melting part of the solution inside the microchannels which will block or open the transport pathway.

The fourth embodiment of the present invention describes the modulation of transport flow inside of the microchannels by modifying the properties of the microchannel surface. In one preferable aspect the composition of the interior part of the microfluidic device contains material which when exposed to solution will provide additional functions such as charge, hydrophobicity, affinity, recognition, sensing and catalytic elements. In some aspects the introduction of affinity or recognition functions can be achieved by the introduction into the composition of the interior part and / or by the immobilisation onto the top, bottom or side part of the microfluidic device a protein, biological receptor, nucleic acid, chromosome, cell, virus, microorganism, tissue sample, carbohydrate, oligosaccharide, polysaccharide, nucleoprotein, mucoprotein, lipoprotein, synthetic protein, glycoprotein, glucosaminoglycan, steroid, immunosuppressant, hormone, heparin, antibiotic, vitamin or drug. Upon melting part of the introduced material will be exposed to the solution providing an interacting point for selective binding, recognition or modulation of the solution properties. In another aspect the introduction of affinity or recognition functions can be achieved by filling the microchannel or reservoir with solution, suspension or emulsion of a corresponding molecule, oligomer, polymer, tissue or cell and by freezing part of it in order to achieve an entrapment of these species into the walls of the microchannels or reservoirs.

The fifth embodiment of the present invention describes the application of flexible microfluidic devices. These devices will be used in a variety of applications, including, e.g., high throughput screening assays in drug discovery, immunoassays, diagnostics, genetic analysis, and the like. In another aspect the invented microfluidic device will be used as a reagent mixing apparatus, lab-on-a-chip for performing chemical and / or biological experiments and as research platform for studying and optimising microfluidic processes.

While advantageous embodiments have been chosen to illustrate the invention, it will be understood by those skilled in the art that various changes and modifications can be made therein without departing from the scope of the invention as defined in the corresponding embodiments.

References

Patent	Country	Issued	Title
6,379,974	USA	April 30, 2002	Microfluidic systems
6,344,326	USA	February 5, 2002	Microfluidic method for nucleic acid purification and processing
6,342,142	USA	January 29, 2002	Apparatus and method for performing microfluidic manipulations for chemical analysis
6,309,602	USA	October 30, 2001	Stacked, reconfigurable system for electrophoretic transport of charged materials
6,251,343	USA	June 26, 2001	Microfluidic devices and systems incorporating cover layers
5,637,469	USA	June 10, 1997	Method and apparatus for the detection of an analyte utilizing mesoscale flow system
5,498,392	USA	March 12, 1996	Mesoscale polynucleotide amplification device and method
4,908,112	USA	March 13, 1990	Silicon semiconductor wafer for analyzing micronic biological samples

Other references:

1. Doherty et al. LC-GC (1994), 12, 846-850.
2. Manz et al. Trends in Anal. Chem. (1990), 10, 144-149 and Manz et al. Adv. in Chromatog. (1993), 33, 1-66.

Reconfigurable microfluidic device

ABSTRACT: The present invention generally provides microfluidic devices comprising a body structure which has a plurality of ports disposed in its structure and a microscale channel network disposed therein. Each port being in fluid communication with one or more channels in the channel network. The subject devices find use in a variety of electrophoretic applications, including clinical assays, high throughput screening for genomics, proteomics and pharmaceutical applications, point-of-care in vitro diagnostics, molecular genetic analysis and nucleic acid diagnostics, cell separations, and bioresearch generally.

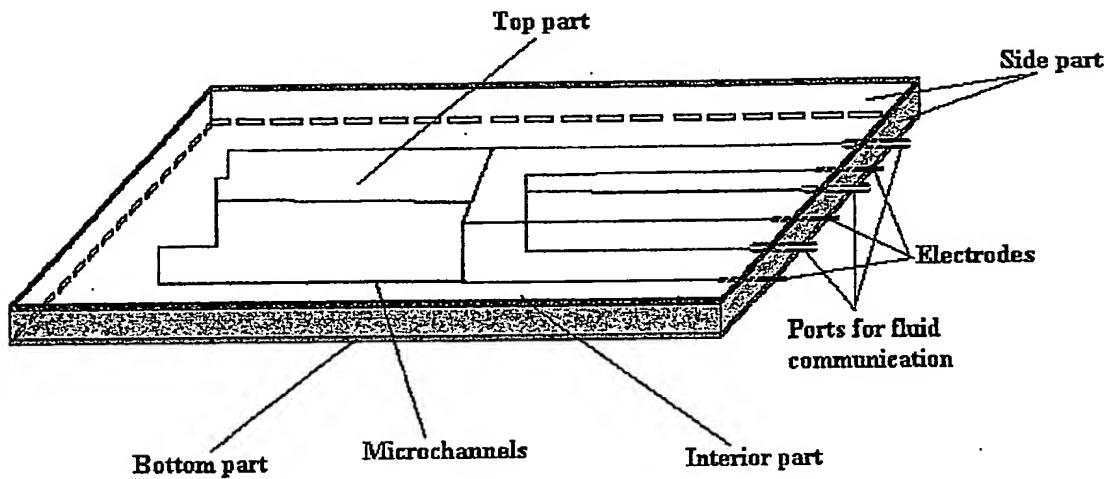


FIGURE 1. Schematic view of a microfluidic device according to a first preferred embodiment of the present invention.

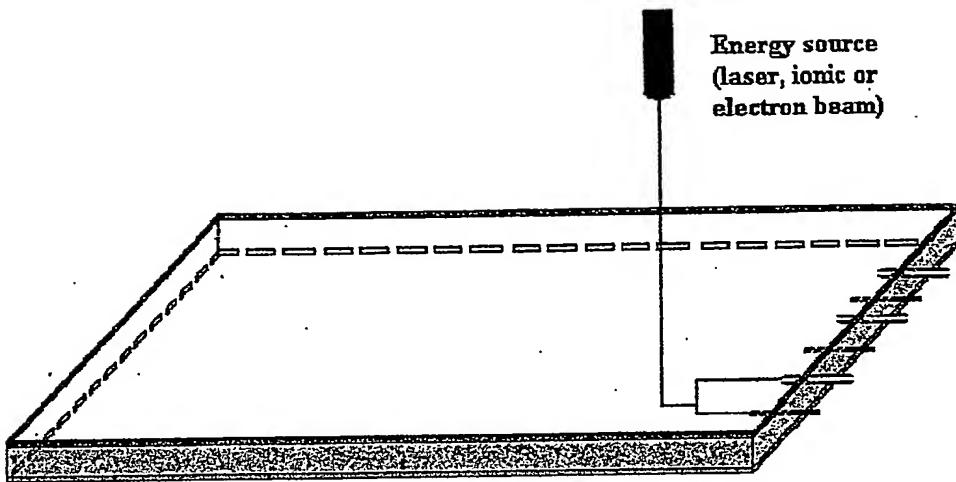


FIGURE 2. Formation of microchannel network in the interior part of the microfluidic device according to a second preferred embodiment of the present invention. Fluctuating laser (electronic or ionic beam) according to pattern, defined by e.g. computer software, melts the substrate material of interior part of the microfluidic device and creates microchannels.

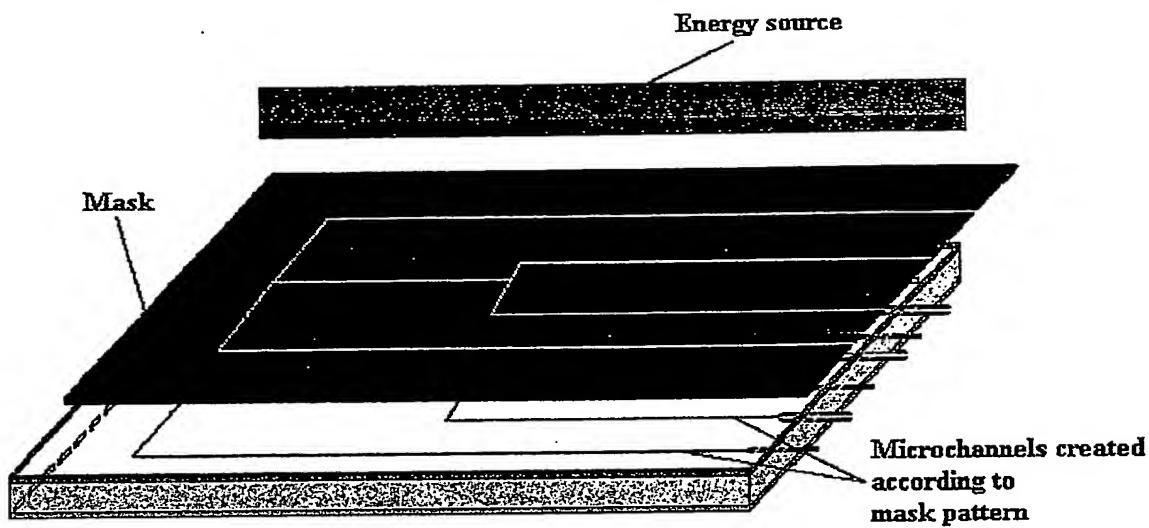


FIGURE 3. Formation of microchannel network into the interior part of the microfluidic device. The energy flow emitted from broad energy source and patterned by mask melts the substrate material of interior part of the microfluidic device and creates microchannels.

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